

REMARKS

Claims status and formal matters

Claims 1, 3, 4, 6, 8, 9, 10, 26, 27, 28, 29, 30, 34 are currently amended. Claims 11-24 have been withdrawn by the Examiner. Claims 7 and 33 are canceled without prejudice to applicants' right to pursue the subject matter of these claims in a future application. Claims 35, 36, 37 and 38 are new.

These amendments raise no issue of new matter. Support for the amendments in claims 3, 6 and 26 can be found, *inter alia*, in the specification as filed. For example, support can be found in Examples 2 and 3 of the specification as originally filed. Support for claims 35 and 37 can be found, *inter alia*, in Example 3, paragraph [0056], and SEQ ID NOS:6, 10, 13, 16. Support for claim 38 can be found, *inter alia*, in Example 2, paragraph [0053] and FIG.2, and Example 3, including FIG. 4A and FIG. 4B.

Objections

Specification

The Examiner stated that the specification contains sequence recitations, for example on pages 16 and 20, without proper reference to SEQ ID NOS as identifiers. The Examiner further stated that inspection of the sequence listing indicates that some or all of these sequences are absent from the listing.

In reply, applicants have amended the specification to include the SEQ ID NOS, and have submitted a complete Sequence Listing, including a paper copy, a computer readable copy and a statement under 37 C.F.R. § 1.821 (f) (attached herein).

Drawings

The Examiner objected to the drawings because Figure 4 was filed as a color drawing. In reply, applicants have submitted herewith a replacement drawing.

Rejections Under 35 U.S.C. §112

The Examiner rejected claims 1-10, 25-34 under 35 U.S.C. §112. The Examiner stated that claims 1, 4, 7, 8, 27, 29, 33 are indefinite because the open meaning of comprising conflicts the closed range of 10-30 nucleotides in the recitation “comprising 10-30 consecutive nucleotides”. Currently amended claims recite the phrase “consisting of from about 10 to about 30 consecutive nucleotides”. Therefore, applicants respectfully request withdrawal of this rejection.

The Examiner stated that claims 3, 6, and 26 are incomplete for lack of recitation of an active step. The Examiner alleges that claims 33 and 34, which lack a detection and correlation step are also incomplete. Currently amended claims 3, 6, 26 and 34 all recite a number of steps including an amplification and detection step. Although the currently amended claims do not explicitly recite a correlation step, the detection step allows for determination whether the sample contains SARS nucleic acids or not. As demonstrated in Example 2 and the results presented in FIG. 2, only the primers of the instant invention allow for product amplification without the requirement for nesting. Applicants maintain that the claims as amended are complete in their recitation of the method and respectfully requests withdrawal of this rejection.

Claims 9, 10, 28, 30 are allegedly indefinite because of the recitation “fragment, variant, and derivative”. Currently amended claims 9, 10, 28, 30 do not contain this recitation and therefore, applicants respectfully request withdrawal of this rejection.

Rejections Under 35 U.S.C. §102

Fodor et al. US Publication 2001/0053519

The Examiner rejected claims 1-10, 25 and 26 as being anticipated under 35 U.S.C. §102(b) by Fodor et al. According to the Examiner, Fodor et al. teaches an array which comprises every possible sequence of 10 residues of DNA. The Examiner states that the complete set of 10-mers necessarily and inherently comprises all of the 10-mers of claims 1, 4, and 7, and any possible set of 10-mers of claim 8.

In reply, applicants traverse the rejection. First, Fodor et al. discloses the concept of using a formula to provide 10-mer nucleic acids. Fodor discloses the theoretical idea of an array and provides a mathematical formula that represents the 10-mers in the array: 4^n where $n=10$ which gives a total of 1,048,576 nucleic acid sequences. Fodor et al. does not disclose the actual nucleic sequence of **any** of these 1,048,576 nucleic acids. Fodor et al. does not disclose a nucleic acid, which has a sequence as recited in claims 1, 4, 7, and 8, or indeed any nucleic acid sequence. Clearly, Fodor et al. does not disclose a synthetic nucleic acid or the specific sequences from about 10 to about 30 consecutive nucleotides of SEQ ID NO:1 as claimed herein.

Second, MPEP 2131.02 recites: "A generic chemical formula will anticipate a claimed species covered by the formula when the species can be "at once envisaged" from the formula. When a compound is not specifically named, but instead it is necessary to select portions of teachings within reference and combine them,, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated....One of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds included in the generic formula before any of the compounds can be "at once envisaged.""

A nucleic acid is a polymer, which can be described by a chemical formula. Fodor et al. discloses a generic chemical formula of a polymer, which has 10 different positions that can be substituted by different nucleic acids. Fodor et al. does not teach the nucleic acid sequence of every possible 10-mer. Applicant argues that looking at the disclosure of Fodor et al., one of ordinary skill in the art cannot simply envision the nucleic acids sequences of the instant invention among the 1,048,576 possible combinations suggested in Fodor et al. Furthermore, Example 2 on page 12 referred to by the Examiner, fails to describe a preferred embodiment that further limits the possible substituents and thus fails to describe the nucleic acids of the instant invention.

For all the reasons stated above, Fodor et al. does not anticipate the claimed invention. Applicants respectfully request withdrawal of the rejection of independent claims 1, 4, 7 and 8, and all dependent claims therefrom.

The Examiner also rejected claims 3, 6, and 26 as allegedly anticipated by Fodor et al. that discloses the use of an array, which can constitute a kit. In reply, Applicant traverses and states

that currently amended claims 3, 6, and 26 recite method steps, which are not disclosed in Fodor et al. Furthermore, Fodor et al. does not anticipate the claimed nucleic acids for the reasons stated above. Therefore, applicants respectfully request withdrawal of this rejection.

Genbank locus AY274119

The Examiner stated that claims 1, 4, 7-10 are anticipated under 102(a) by Genbank locus AY274119. The Genbank entry involves the entire sequence of the SARS genome as of April 14, 2003. The Examiner also contends that the web-site "SARS-associated Coronavirus" had similar sequence data publicly available 2 days earlier. Both references cited by the Examiner involve the complete nucleic acid sequence of the SARS-associated Coronavirus. Neither one of these two reference teaches a synthetic nucleic acid as claimed. Therefore, applicants respectfully request withdrawal of this rejection.

Rejections Under 35 U.S.C. §103

Fodor et al. US 2001/0053519

The Examiner rejected claims 27-32 under 35 U.S.C. §103(a) as being unpatentable over Fodor et al. since claims 27-32 differ from Fodor et al. in requiring instructions for use and requiring PCR reagents.

In reply, applicants traverse the rejection. Fodor et al. does not disclose or make obvious the claimed nucleic acids included in the claimed kits for the reasons stated above. Withdrawal of the rejection is respectfully requested.

Combined teachings of Ksiazek et al. (2003), Genbank locus AY274119 and either Vabret et al. (2001) or Stewart et al. (1995)

The Examiner rejected claims 1-10, 25-34 as allegedly unpatentable over the combined teachings of Ksiazek et al. (2003) New England Journal of Medicine 348(20):1953-1966, published online on April 10 (the Ksiazek reference), Genbank Accession AY274119 and either Vabret et al. (2001) Journal of Virological Methods 97:59-66 (The Vabret reference) or Stewart et al. In:

Y.Becker and G.Darai,Eds, Diagnosis of Human Viruses by Polymerase Chain Reaction Technology, Springer-Verlag, New York (1995), pp.316-327 (the Stewart reference).

Ksiazek et al. (2003) and Genbank locus AY274119

The Ksiazek reference discloses amplification of a nucleotide segment of coronavirus associated with SARS using primers in the polymerase gene. The Genbank sequence discloses the nucleic acid sequence of the SARS genome.

Vabret et al. 2001 or Stewart et al. 1995

The Vabret reference discloses primers in the M gene region of coronaviruses HcoV-229E (type I coronavirus) and HcoV-OC43 (type II coronavirus), wherein the sensitivity of M gene primers is compared to known primers in the N gene. The Stewart reference involves primers in the N gene region of HcoV-229E and HcoV-OC43 coronaviruses.

In reply, applicant traverses the rejection. First, the Ksiazek reference does not teach or suggest the use of PCR primers located in any other portion of the SARS genome. As stated above, the Genbank sequence discloses the nucleic acid sequence of the SARS genome and does not teach or suggest synthetic nucleic acids in the N gene or the 3' noncoding region. Therefore, neither Ksiazek nor Genbank locus provides motivation to combine their teaching with Vabret or Stewart.

Second, neither reference teaches any primers from the 3' noncoding region of a coronavirus. Furthermore, neither Vabret nor Stewart teaches any nucleic acids from the SARS genome since the SARS virus and its genome were not identified until April 2003. Therefore, the Ksiazek or Genbank locus reference, in view of Vabret or Stewart, does not teach or suggest primers from the 3' non-coding region of SARS corona virus as claimed.

Third, SARS coronavirus is genetically distinct and phylogenetically distant from other coronaviruses (see section Molecular analysis on page 1958 and Figure 3 in the Ksiazek reference). The often fastidious nature of nucleic acid hybridization, and PCR amplification of

nucleic acids from genomic nucleic acids is well known to artisans skilled in the art. Given the distant relationship between the SARS virus genome and the genomes of type I and II coronaviruses, there was no expectation that primers designed in the N region of the SARS virus will successfully amplify nucleic acid sequences from the SARS genome. Having the knowledge of successful use of the claimed primers the Examiner is using the benefit of hindsight to argue that it was obvious to combine Ksiazek or Genbank locus with Stewart or Vabret.

Fourth, the Vabret reference teaches primers in the M gene region of coronaviruses HcoV-229E and HcoV-OC43, wherein the sensitivity of M gene primers is compared to known primers in the N gene. Applicants point out that the Vabret reference does not teach or suggest primers in the N gene region and that the Vabret reference teaches away from using primers in N gene region. The Examiner's attention is drawn to the statement on page 63, first complete paragraph in the right column: "For HcoV-OC43, RT-PCR hybridization with the primers defined in the N gene by Myin et al. (1994) and Stewart et al. (1995) are not sensitive." The Vabret reference discloses that M gene primers allow higher sensitivity level of detection and therefore are preferred to primers in the N gene. Thus a person skilled in the art will be discouraged from using primers in the N region. Therefore, the Ksiazek reference in view of the Vabret reference does not teach or suggest the primers of the instant invention.

Fifth, the Stewart reference teaches primers derived from the N gene region of coronaviruses HcoV-229E and HcoV-OC43. The primers of the instant invention, which are derived from the SARS coronavirus, have nucleic acid sequences which are different from the primers in the Stewart reference which are derived from coronaviruses HcoV-229E and HcoV-OC43. The nucleotide sequence of type I and II coronaviruses are different from the SARS virus. Therefore, it would not have been obvious to obtain primers from the N gene of the SARS coronavirus in view of Stewart and Ksiazek et al. and Genbank locus AY274119, since the nucleotide sequences of the SARS coronavirus and type I and type II viruses are different, and since the SARS virus is classified as genetically distinct from other known coronaviruses. Furthermore, the method of virus detection described by the Stewart reference requires two distinct steps: RT-

PCR amplification followed by Southern blot hybridization of the PCR product to radio-actively labeled probes. This two-step detection method is fundamentally different from the one step PCR amplification detection of the SARS virus afforded by the primers and methods as claimed.

In view of the foregoing, applicants argue that neither the Ksiazek reference or Genbank sequence in view of either Stewart or Vabret teaches or suggests the synthetic nucleic acids sequences as claimed. Withdrawal of the rejections is respectfully requested.

CONCLUSION

For the reasons stated above, applicants request that the Examiner withdraw the grounds for rejection and allow the pending claims to proceed to issue. If the Examiner has any questions, she is invited to call the undersigned attorney.

Authorization is given to apply any charges that may be due, or any credits owed, to Deposit Account No. 08-0219.

Respectfully submitted,



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